Green and solvent-free procedure for microwave-assisted synthesis of 2,4,6-triarylpyridines catalysed using MgAl_2O_4 nanocrystals

JAVAD SAFARI*, SOHEILA GANDOMI-RAVANDI and MAHMOUD BORJIAN BORUJENI

Laboratory of Organic Chemistry Research, Department of Chemistry, College of Chemistry,
University of Kashan, Kashan, P.O. Box: 87317-51167, Kashan, Islamic Republic of Iran
e-mail: Safari@kashanu.ac.ir

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Abstract. Design and development of a heterogeneous nanocatalyst for condensation reaction of acetophenone derivatives, aromatic aldehydes, and ammonium acetate to yield 2,4,6-triarylpyridines followed by microwave irradiation is described. Nanocrystalline MgAl_2O_4 as a novel heterogeneous recyclable catalyst shows high activity for the above reaction. In addition, the easily recoverable nanosized catalysts showed good reusability.

Keywords. Triarylpyridine; microwave irradiation; multi-component reaction; heterogeneous catalyst.

1. Introduction

Microwave technology is recognized as a very important tool in organic synthesis and therefore microwave chemistry can provide access to synthetic transformations.¹ Microwave heating is observed to yield a number of unique advantages including non-contact and uniform heating, rapid and selective heating, volumetric heating, reduced processing costs, quick start-up and stopping.² Furthermore, reactions under microwave have the great advantage of not using organic solvents (solvent-free), and thus such reactions are more environment-friendly and generate less waste. It has been well-established that microwaves shorten reaction time and improve product yield without the use of solvents.^{3–5} N-heterocyclic compounds, such as pyridines have a unique position in synthetic chemistry. The pyridyl heterocyclic nucleus is a building block in molecules of natural products, pharmaceuticals such as vasodilator, anticonvulsant, antiepileptic, anaesthetic and agrochemicals such as pesticides and herbicides.^{6–9} Owing to their π -stacking ability, directional H-bonding and coordination, triarylpyridines are widely used in supramolecular chemistry.¹⁰ Previously, 2,4,6-triarylpyridines (Krohnke pyridine) were prepared through the reaction of *N*-phenacylpyridinium salts with α,β -unsaturated ketones in the presence of NH_4OAc ,^{11,12} the condensation of 1,5-diketones with formamide-ammonium formate¹³ and by other synthetic procedures including the Chichibabin

method.^{14–17} More recently, many improved methods and procedures for preparation of 2,4,6-triarylpyridines have been reported such as reaction of α -ketoketene dithioacetals with methyl ketones,¹⁸ reaction of *N*-phosphinyloethanimines with aldehydes,¹⁹ reaction of chalcones with ammonium acetate,²⁰ addition of lithiated β -enamino phosphonates to chalcones,²¹ reaction of chalcones and compounds possessing terminal $-\text{CXNH}_2$ functionality,^{22,23} reaction of acetophenone and chalcone with a source of ammonia (urea, ammonium acetate, and guanidine),^{24–26} and condensation of acetophenones, benzaldehydes and NH_4OAc .²⁷ Among all these methods, one-pot condensation reaction of acetophenones with aryl aldehydes, and ammonium acetate is a well-established protocol for the synthesis of 2,4,6-triarylpyridines. This one-pot condensation has been developed in the presence of catalytic amount of acetic acid,²⁰ NaOH in PEG-400,²⁸ Preyssler type heteropolyacid $\text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$,²⁹ Bronsted acidic ionic liquid,³⁰ $\text{HClO}_4\text{-SiO}_2$,³¹ cyanuric chloride,³² I_2 ,³³ wet 2,4,6-trichloro-1,3,5-triazine (TCT),³² pentafluorophenylammonium triflate (PFPAT),³⁴ $\text{Bi}(\text{OTf})_3$,³⁵ $\text{H}_2\text{SO}_4\text{-SiO}_2$,³⁶ tetrabutylammonium hydrogen sulphate (TBAHS),³⁷ PPA-SiO_2 ,³⁸ and *N*-bromosuccinimide or trichloroisocyanuric acid.³⁹ In recent years, nano materials have emerged as powerful catalysts in various organic transformations such as ZnO nanoparticles,⁴⁰ barium chloride dispersed on silica gel nanoparticles⁴¹ for synthesis of 2,4,6-triarylpyridines, and using silica nanoparticles for preparation of highly substituted pyridines.⁴² The nanosized spinel particles have many applications because of their good physical and

*For correspondence

Scheme 1. Microwave-mediated synthesis of 2,4,6-triarylpyridines in the presence of nanocrystalline MgAl_2O_4 .

chemical properties.⁴³ Magnesium aluminate spinel (MgAl_2O_4) is one of the best known and widely used materials. It has good thermal shock resistance and high chemical inertness in both basic and acidic environments.^{44,45} Moreover, spinel has found application in catalyst support,⁴⁶ dentistry, humidity sensors⁴⁷ and ceramic pigments.⁴⁸ However, to the best of our knowledge, the use of MgAl_2O_4 as catalyst in the synthesis of 2,4,6-triarylpyridines has not been reported. Herein, we introduce a simple, easy and one-pot synthesis for 2,4,6-triarylpyridines using nanocrystalline MgAl_2O_4 as a novel heterogeneous catalyst under microwave conditions (Scheme 1).

2. Experimental

2.1 Materials and instruments

All materials were purchased from Merck and Fluka in commercial grade. All yields refer to isolated products. Melting points were recorded on an electrothermal 9200 MK3 melting point. The FT-IR spectra were obtained on a Nicolet Magna 550 Fourier transform infrared (FT-IR) spectrophotometer as KBr disk. Elemental analyses were determined by using a Perkin–Elmer 2400 CHNS/O analyser instrument. Chemical ionization mass spectral data were obtained using a Micro Mass UK LTD mass spectrometer. The ^1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra (400 MHz, 100 MHz) were recorded on a Bruker Avance–DRX–400 spectrometer using Dimethyl sulfoxide ($\text{DMSO}-d_6$) as solvent and Tetramethylsilan (TMS) as an internal standard. The CEM–Discover Focused Monomode Microwave reactor (2450 MHz, 300 W) was used for microwave irradiation. Microwave-mediated reactions were performed in sealed process vials under air with magnetic stirring.

2.1a General method for synthesis of nano crystalline MgAl_2O_4 : $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ were used as starting materials. Stoichiometric amounts of magnesium and aluminum nitrates were added to

well-stirred deionized water. Ethylene diamine was added dropwise to the well-stirred slurry for adjusting pH value to around 9. After precipitation, the slurry was stirred for another 30 min and then stirred at 80°C for 24 h under reflux conditions. Finally, the product was filtered and dried at 100°C for 24 h under flowing air and calcined at 700° and 800°C for 5 h. This method was obtained from literature.²⁰

2.1b General method for one-pot synthesis of 2,4,6-triarylpyridines under microwave irradiation: Aromatic aldehydes (1 mmol), acetophenones (2 mmol), NH_4OAc (4 mmol), and nanocrystalline MgAl_2O_4 (5 mol%) were heated in a microwave oven for an appropriate time. Upon completion, hot ethanol was added to the mixture and the insoluble catalyst was filtered off. The pure products were obtained by recrystallization from 95% ethanol. The structures of the products **4a–q** were deduced from their IR, ^1H and ^{13}C NMR, MS and CHN analysis spectra.

2.2 Spectral data

2.2a 2,4,6-Triphenylpyridine ($\text{C}_{23}\text{H}_{17}\text{N}$ **4a):** White solid; m.p. $135\text{--}137^\circ\text{C}$ (85%); R_f (petroleum ether: ethylacetate): 7:3 (v/v) = 0.80; UV (CHCl_3) λ_{max} = 304 nm; FT-IR (KBr) = 3069, 1597, 1552, 1494, 1440, 1398, 1178, 1074, 1027, 867, 759, 692 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.33–8.37 (d, 4H, ArH), 8.20 (s, 2H, ArH), 8.02–8.07 (d, 2H, ArH), 7.50–7.60 (m, 9H, ArH); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 157.02, 150.06, 139.26, 139.19, 129.73, 129.68, 128.72, 128.39, 127.75, 127.4, 117.02; Mass (ES-MS): m/z 308.1 (M^+); Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{N}$: C 89.87, H 5.57, N 4.56; found: C 89.54, H 5.42, N 4.67%.

2.2b 4-(4-Chlorophenyl)-2,6-diphenylpyridine ($\text{C}_{23}\text{H}_{16}\text{ClN}$ **4b):** White solid; m.p. $127\text{--}128^\circ\text{C}$ (87%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl_3) λ_{max} = 304 nm; FT-IR (KBr) = 3061, 1599, 1543, 1489, 1449, 1414, 1384, 1237, 1090, 1013, 825, 773, 692 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.33–8.38 (d, 4H, J = 7.2 Hz, ArH), 8.14 (s, 2H, ArH), 7.78 (d, 2H, J = 8 Hz, ArH), 7.62–7.650 (d, 2H, J = 6.8 Hz, ArH), 7.53–7.56 (m, 6H, J = 8 Hz, ArH); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 157.05, 148.64, 139.18, 136.94, 134.7, 129.64, 129.47, 129.44, 129.17, 116.88; Anal. Calcd. for $\text{C}_{23}\text{H}_{16}\text{ClN}$: C 80.81, H 4.72, N 4.10, Cl 10.37; Found C 80.73, H 4.61, N 4.07, Cl 10.30.

2.2c 4-(3-Methoxyphenyl)-2,6-diphenylpyridine ($\text{C}_{24}\text{H}_{19}\text{NO}$ **4c):** White solid; m.p. 124–127°C (85%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl_3) λ_{max} = 308 nm; FT-IR (KBr) = 3034, 1596, 1547, 1486, 1444, 1398, 1285, 1255, 1204, 1171, 1037, 872, 775, 692 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.30–8.36 (d, 4H, J = 7.6 Hz, ArH), 8.14 (s, 2H, ArH), 7.50–7.59 (m, 8H, J = 7.6 Hz, ArH), 7.45–7.48 (d, 1H, J = 6.8 Hz, ArH), 7.06–7.08 (d, 1H, J = 6.8 Hz, ArH), 3.82 (s, 3H, OCH_3); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 160.37, 156.97, 150.02, 139.76, 139.27, 130.63, 129.67, 129.18, 127.45, 120.09, 117.2, 115.39, 113.22, 55.79; GCMS (EI): m/z (%) 337.15 (100) $[\text{M}]^+$; Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{NO}$: C 85.43, H 5.68, N 4.15, O 4.74; found: C 85.51, H 5.59, N 4.25, O 4.65%.

2.2d 4-(2-Fluorophenyl)-2,6-diphenylpyridine ($\text{C}_{23}\text{H}_{16}\text{FN}$ **4d):** White solid; m.p. 119–120°C (88%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl_3) λ_{max} = 260 nm; FT-IR (KBr) = 3031, 1591, 1544, 1490, 1451, 1395, 1288, 1209, 1204, 1114, 1074, 1025, 878, 759, 694 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.32–8.36 (d, 4H, ArH), 8.10 (s, 2H, ArH), 7.83–7.87 (t, 1H, ArH), 7.45–7.48 (d, 1H, ArH), 7.06–7.085 (d, 1H, ArH); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 160.37, 156.97, 150.02, 139.76, 139.27, 130.63, 129.67, 129.18, 127.45, 120.09, 117.2, 115.39, 113.22, 55.79; GCMS (EI) m/z (%) 325.13 (100) $[\text{M}]^+$; Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{NO}$: C 84.90, H 4.96, F 5.84, N 4.30; found: C 85.01, H 4.85, F 5.78, O 4.36%.

2.2e 4-(5-Methylfuran-2-yl)-2,6-diphenylpyridine ($\text{C}_{22}\text{H}_{17}\text{NO}$ **4e):** Light brown solid; m.p. 162–164°C (85%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl_3) λ_{max} = 260 nm; FT-IR (KBr) = 3058, 2927, 1591, 1548, 1495, 1447, 1394, 1237, 1122, 1204, 1114, 1075, 1027, 878, 758, 691 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.24–8.29 (d, 4H, ArH), 8.10 (s, 2H, ArH), 7.47–7.57 (m, 7H, ArH), 6.34 (s, 1H, ArH), 2.50 (s, 3H, ArH); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 155.30, 151.40, 146.10, 136.20, 129.30, 127.60, 127.40, 118.60, 107.80, 101.80, 14.10; GCMS (EI) m/z (%) 311.13 (100) $[\text{M}]^+$; Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{NO}$: C 84.86, H 5.50, N 4.50, O 5.14; found: C 84.91, H 5.45, N 4.54, O 5.10%.

2.2f 4-(Furan-2-yl)-2,6-diphenylpyridine ($\text{C}_{21}\text{H}_{15}\text{NO}$ **4f):** Light brown solid; m.p. 168–170°C (88%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.82; UV (CHCl_3) λ_{max} = 260 nm; FT-IR (KBr) = 3058, 1606, 1541, 1487, 1454, 1414, 1244, 1158, 1073, 1010, 868,

772, 690 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.24–8.29 (d, 4H, ArH), 8.13–8.15 (s, 2H, ArH), 7.93–7.96 (s, 1H, ArH), 7.47–7.57 (m, 7H, ArH), 6.74–6.75 (d, 1H, J = 1.6 Hz, ArH); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 110.85, 112.95, 113.08, 127.23, 129.22, 129.8, 130.01, 139.55, 145.23, 151.43, 156.97; Anal. Calcd. for $\text{C}_{21}\text{H}_{15}\text{NO}$: C 84.82, H 5.08, N 4.71, O 5.38; Found C 84.86, H 5.01, N 4.77, O 5.42.

2.2g 2,6-Diphenyl-4-p-tolylpyridine ($\text{C}_{24}\text{H}_{19}\text{N}$ **4g):** White solid; m.p. 118–119°C (88%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.8; UV (CHCl_3) λ_{max} = 304 nm; FT-IR (KBr) = 3034, 2936, 1598, 1548, 1442, 1398, 1286, 1254, 1203, 1170, 1036, 871, 775, 691 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.29–8.3 (d, 4H, J = 7.2 Hz, ArH), 8.14 (s, 2H, ArH), 7.92–7.94 (d, 2H, J = 7.6 Hz, ArH), 7.51–7.55 (t, 4H, J = 7.2 Hz, ArH), 7.46–7.48 (t, 2H, J = 7.2 Hz, ArH), 7.34–7.36 (d, 2H, J = 7.6 Hz, ArH), 2.48 (s, 3H, CH_3); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 156.96, 149, 139.41, 135.18, 130.14, 129.63, 129.17, 127.54, 127.38, 116.66, 21.25; Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{N}$: C 89.68, H 5.96, N 4.36; Found C 89.62, H 5.90, N 4.32.

2.2h 4-(4-Methoxyphenyl)-2,6-diphenylpyridine ($\text{C}_{24}\text{H}_{19}\text{NO}$ **4h):** White solid; m.p. 98–100°C (80%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.8; UV (CHCl_3) λ_{max} = 301 nm; FT-IR (KBr) = 3035, 2936, 1596, 1547, 1486, 1444, 1398, 1285, 1255, 1204, 1171, 1037, 750, 691 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.30–8.38 (d, 4H, J = 7.2 Hz, ArH), 8.14 (s, 2H, ArH), 8.02–8.04 (d, 2H, J = 8 Hz, ArH), 7.53–7.59 (t, 4H, J = 7.2 Hz, ArH), 7.46–7.49 (d, 2H, J = 6.8 Hz, ArH), 7.09–7.15 (d, 2H, J = 8 Hz, ArH), 3.82 (s, 3H, CH_3); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 160.83, 156.90, 149.54, 139.40, 130.40, 130.27, 129.61, 129.11, 127.39, 116.38, 114.95, 55.80; Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{NO}$: C 85.43, H 5.68, N 4.15, O 4.74; Found C 85.49, H 5.64, N 4.10, O 4.78.

2.2i 4-(2,6-Diphenylpyridin-4-yl)-N,N-dimethylbenz-enamine ($\text{C}_{25}\text{H}_{22}\text{N}_2$ **4i):** Yellow solid; m.p. 137–139°C (86%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl_3) λ_{max} = 252 nm; FT-IR (KBr) = 3037, 2936, 1598, 1525, 1489, 1442, 1398, 1352, 1233, 1199, 1168, 1066, 1023, 818, 773, 695 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.27–8.30 (d, 4H, J = 7.2 Hz, ArH), 8.10 (s, 2H, ArH), 7.90–7.93 (d, 2H, J = 8.4 Hz, ArH), 7.44–7.55 (m, 6H, ArH), 6.82–6.84 (d, 2H, J = 8.4 Hz, ArH), 3.19 (s, 3H, CH_3); ^{13}C NMR (100 MHz $\text{DMSO}-d_6$): δ 155.20, 152.00,

150.10, 136.20, 129.30, 128.30, 127.60, 127.40, 118.00, 114.80, 40.20; Anal. Calcd. for $C_{25}H_{22}N_2$: C 85.68, H 6.33, N 7.99; Found C 85.62, H 6.29, N 7.94.

2.2j 2,6-Bis (4-chlorophenyl)-4-phenylpyridine ($C_{23}H_{15}Cl_2NO$ **4j**): White solid; m.p. 175–178°C (88%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3052, 1598, 1544, 1490, 1449, 1413, 1384, 1239, 1174, 1091, 1012, 829, 761, 694 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.34–8.41 (d, 4H, ArH), 8.23 (s, 2H, ArH), 8.03–8.06 (d, 2H, ArH), 7.50–7.61 (m, 7H, ArH); ^{13}C NMR (100 MHz DMSO- d_6): δ 155.75, 150.31, 137.86, 134.65, 129.91, 129.55, 127.87, 117.31; Anal. Calcd. for $C_{23}H_{15}Cl_2NO$: C 70.42, H 3.85, N 3.57, Cl 18.07, O 4.08; Found C 70.36, H 3.80, N 3.51, Cl 18.01, O 4.04.

2.2k 2,6-Bis (4-chlorophenyl)-4-(4-methoxyphenyl)pyridine ($C_{24}H_{17}NOCl_2$ **4k**): White solid; m.p. 190–191°C (88%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3052, 2928, 1602, 1543, 1512, 1489, 1426, 1381, 1291, 1247, 1177, 1088, 1011, 824 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.29–8.40 (d, 4H, J = 7.2 Hz, ArH), 8.17 (s, 2H, ArH), 8.50–8.60 (d, 4H, J = 7.2 Hz, ArH), 7.45–7.50 (d, 2H, J = 6.8 Hz, ArH), 7.09–7.12 (d, 2H, J = 8 Hz, ArH), 3.84 (s, 3H, CH_3); ^{13}C NMR (100 MHz DMSO- d_6): δ 161.10, 155.75, 134.30, 132.90, 130.20, 129.3, 129, 128.40, 118, 114.80, 5.80; Anal. Calcd. for $C_{24}H_{17}NOCl_2$: C 70.95, H 4.22, N 3.45, O 3.94, Cl 17.45; Found C 70.91, H 4.25, N 3.41, O 3.97, Cl 17.40.

2.2l 2,6-Bis (4-chlorophenyl)-4-(2-methoxyphenyl)pyridine ($C_{24}H_{17}Cl_2NO$ **4l**): White solid; m.p. 164–166°C (86%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3049, 2948, 1601, 1542, 1512, 491, 1411, 1383, 1263, 1245, 1175, 1126, 1090, 1014, 827, 749 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.22–8.32 (d, 4H, J = 8 Hz, ArH), 8.04 (s, 2H, ArH), 7.53–7.63 (d, 5H, J = 8 Hz, ArH), 7.43–7.45 (t, 1H, J = 8 Hz, ArH), 7.18–7.22 (d, 1H, J = 8 Hz, ArH), 7.09–7.14 (t, J = 8 Hz, 1H, ArH), 3.84 (s, 3H, CH_3); ^{13}C NMR (100 MHz DMSO- d_6): δ 161.10, 155.75, 134.30, 132.90, 130.20, 129.3, 129, 128.40, 118, 114.80, 55.80. GCMS (EI) m/z (%): 405.07 (100) $[M]^+$; Anal. Calcd. for $C_{24}H_{17}Cl_2NO$: C 70.95, H 4.22, Cl 17.45, N 3.45, O 3.94; found: C 71.03, H 4.18, Cl 17.36, N 3.51, O 3.92%.

2.2m 2,6-Bis (4-chlorophenyl)-4-(3-methoxyphenyl)pyridine ($C_{24}H_{17}Cl_2NO$ **4m**): White solid; m.p. 159–160°C (80%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3062, 2932, 1595, 1546, 1490, 1460, 1411, 1383, 1265, 1211, 1176, 1089, 1012, 833, 787 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.31–8.40 (d, 4H, J = 7.6 Hz, ArH), 8.20 (s, 2H, ArH), 7.55–7.59 (d, 6H, J = 7.6 Hz, ArH), 7.42–7.50 (d, 1H, J = 6.8 Hz, ArH), 7.05–7.12 (d, 1H, J = 6.8 Hz, ArH), 3.88 (s, 3H, CH_3); ^{13}C NMR (100 MHz DMSO- d_6): δ 161.20, 155.20, 152, 138.90, 134.30, 132.90, 130.3, 129.3, 129, 119.7, 118, 114.80, 111.1, 55.80; GCMS (EI) m/z (%) 405.07 (100) $[M]^+$; Anal. Calcd. for $C_{24}H_{17}Cl_2NO$: C 70.95, H 4.22, Cl 17.45, N 3.45, O 3.94; found: C 71.03, H 4.18, Cl 17.36, N 3.51, O 3.92%.

2.2n 2,6-Bis (4-chlorophenyl)-4-(2-fluorophenyl)pyridine ($C_{23}H_{14}Cl_2FN$ **4n**): White solid; m.p. 144–148°C (80%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3060, 1603, 1544, 1490, 1460, 1411, 1383, 1265, 1211, 1176, 1089, 1012, 826, 750 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.25–8.31 (d, 4H, J = 8.4 Hz, ArH), 8.20 (s, 2H, ArH), 7.8–7.85 (t, 1H, J = 7.6 Hz, ArH), 7.52–7.60 (d, 5H, J = 8.4 Hz, ArH), 7.35–7.43 (t, 2H, ArH); ^{13}C NMR (100 MHz DMSO- d_6): δ 116.0, 118.0, 124.9, 129.0, 129.3, 130.90, 132.8, 134.3, 152, 155.2, 158.2; Anal. Calcd. for $C_{23}H_{14}Cl_2FN$: C 70.07, H 3.58, Cl 17.98, F 4.82, N 3.55; found: C 70.10, H 3.52, Cl 17.80, F 4.79, N 3.79%.

2.2o 2,6-Bis (4-chlorophenyl)-4-(furan-2-yl)pyridine ($C_{21}H_{13}Cl_2NO$ **4o**): White solid; m.p. 144–146°C (87%); R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV ($CHCl_3$) λ_{max} = 252 nm; FT-IR (KBr) = 3061, 1609, 1544, 1488, 1422, 1374, 1265, 1216, 1176, 1090, 1012, 826, 736 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.27–8.38 (d, 4H, J = 8.4 Hz, ArH), 8.21 (s, 2H, ArH), 7.92–7.98 (s, 1H, ArH), 7.52–7.68 (d, 5H, J = 7.6 Hz, ArH), 6.72–6.8 (d, 1H, J = 4 Hz, ArH); ^{13}C NMR (100 MHz DMSO- d_6): δ 155.3, 154, 146.1, 142.9, 134.30, 132.90, 129.30, 129, 118, 107, 105; GCMS (EI) m/z (%) 365.04 (100) $[M]^+$; Anal. Calcd. for $C_{21}H_{13}Cl_2NO$: C 68.87, H 3.58, Cl 19.36, N 3.82, O 4.37; found: C 69.05, H 3.54, Cl 19.39, N 3.75, O 4.27%.

2.2p 4-(2,6-Bis (4-chlorophenyl)pyridin-4-yl)-N,N-dimethylbenzenamine ($C_{25}H_{20}Cl_2N_2$ **4p**): Yellow solid; m.p. 139–140°C (79%); R_f (petroleum ether:

ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl₃) $\lambda_{\max}$ = 252 nm; FT-IR (KBr) = 3061, 2932, 1597, 1527, 1488, 1432, 1359, 1265, 1189, 1201, 1090, 945, 814 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.31–8.35 (d, 4H, *J* = 8.4 Hz, ArH), 8.12 (s, 2H, ArH), 7.89–7.95 (d, 2H, *J* = 8.8 Hz, ArH), 7.52–7.56 (d, 4H, *J* = 8.4 Hz, ArH), 6.80–6.84 (d, 2H, *J* = 8.4 Hz, ArH), 2.98 (s, 6H, 2CH₃); ¹³C NMR (100 MHz DMSO-*d*₆): δ 155.2, 152, 150.1, 134.3, 132.90, 129, 128.3, 127.4, 118, 114.8, 40.2. GCMS (EI) *m/z* (%) 418.10 (100) [M]⁺; Anal. Calcd. for C₂₅H₂₀Cl₂N₂: C 71.60, H 4.81, Cl 16.91, N 6.68; found: C 71.55, H 4.78, Cl 16.98, N 6.69%.

2.2q 4-(2-Chlorophenyl)-2,6-bis (4-chlorophenyl) pyridine (C₂₃H₁₄Cl₃N **4q**): White solid; m.p. 168–170°C (80%); *R*_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.83; UV (CHCl₃) $\lambda_{\max}$ = 252 nm; FT-IR (KBr) = 3034, 1603, 1544, 1490, 1413, 1383, 1263, 1174, 1090, 1012, 824, 751 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.45–8.49 (d, 4H, ArH), 8.12 (s, 2H, ArH), 7.52–7.58 (d, 4H, ArH), 7.4–7.45 (d, 1H, ArH), 7.32–7.34 (d, 1H, ArH), 7.2–7.24 (t, 1H, ArH), 7.16 (t, 1H, ArH); ¹³C NMR (100 MHz DMSO-*d*₆): δ 155.2, 152, 138.9, 134.3, 132.90, 132.1, 130.7, 129.3, 129, 128.8, 127.4, 118; GCMS (EI) *m/z* (%) 409.02 (100) [M]⁺. Anal. Calcd. for C₂₃H₁₄Cl₃N: C 67.26, H 3.44, Cl 25.90, N 3.41; found: C 67.31, H 3.39, Cl 25.87, N 3.43%.

3. Results and discussion

Targeted compounds **4a–q** were obtained starting from acetophenone (2 mmol) and benzaldehyde (1 mmol) in the presence of ammonium acetate (4 mmol) under microwave conditions as a standard model reaction. Application of the prepared nanostructures (MgAl₂O₄) as a catalyst was evaluated in this reaction. A wide variety of catalysts were employed to improve the yield of 2,4,6-triarylpyridine derivatives **4a–q**. As shown in Table 1, the best catalyst for this reaction is nanocrystalline MgAl₂O₄ which led to 95% yield of the desired product in 10 min. We have started to use nanocrystalline MgAl₂O₄ as an efficient catalyst; since it has strong influence on the specific surface area and this character provides attraction between materials. Then, we have focused on optimizing conditions by using different amounts of MgAl₂O₄ nanocrystals. In the absence of catalyst, the reaction leads to a poor product yield and takes longer time for completion. The use of 5 mol% of the catalyst produced maximum yield (95%). Further amount of catalyst does not increase yield (Table 2).

Table 1. Effect of different catalysts on the reaction.

Entry	Catalyst	Time (min)	Yield (%)
1	KOH	20	70
2	NaOH	21	70
3	K ₂ CO ₃	32	60
4	SbCl ₃	18	68
5	AlCl ₃	20	62
6	Al ₂ O ₃	42	50
7	SbCl ₃ –SiO ₂	20	68
8	MgO	30	60
9	BaO	25	65
10	NaOEt	22	70
11	L-Alanine	25	65
12	Montmorillonite	20	70
13	Nano crystalline MgAl ₂ O ₄	10	95

Table 2. Effect of amount of nanocrystalline MgAl₂O₄ in model reaction.

Entry	Catalyst (mol%)	Time (min)	Yield (%)
1	–	40	15
2	2	20	67
3	3	15	79
4	5	10	95
5	7	10	95

Table 3. Effect of different ammonia sources on the reaction.

Entry	Ammonium source	Time (min)	Yield (%)
1	NH ₄ OAc	15	95
2	(NH ₄) ₂ CO ₃	45	45
3	NH ₄ F	15	72
4	NH ₂ CSNH ₂	65	35
5	NH ₂ COCH ₃	70	64
6	NH ₂ CONH ₂	60	30

Table 4. Optimization of reaction power for synthesis of compound **4a**.

Entry	P (w)	Time (min)	Yield (%)
1	30	55	Trace
2	35	40	35
3	40	28	65
4	45	20	80
5	50	15	95
6	60	15	90

Table 5. Reuse of catalyst in the model reaction.

Entry	1	2	3	4	5
Yield (%)	98	96	95	94	94

Table 6. Solvent-free synthesis of 2,4,6-triarylpyridine derivatives catalysed by MgAl_2O_4 under microwave irradiation.

Entry	R	R'	Product	Yield (%)	M.p. (°C)	
					Found	Reported (lit.)
1	H	H	4a	95	135–137	134–135 ⁴⁹
2	4-Cl	H	4b	89	127–128	124–126 ²⁰
3	3-OMe	H	4c	88	124–127	–
4	2-F	H	4d	91	119–120	–
5	5-Me-furan	H	4e	89	162–164	–
6	$\text{C}_4\text{H}_3\text{O}$ (furan)	H	4f	92	158–160	168–170 ⁴⁹
7	4-Me	H	4g	84	119–120	123–124 ²⁰
8	4-OMe	H	4h	84	98–100	99–101 ²⁰
9	4-N(Me) ₂	H	4i	87	137–139	138–140 ⁴⁹
10	H	4-Cl	4j	90	175–178	188–190 ⁵⁰
11	4-OMe	4-Cl	4k	86	190–191	–
12	2-OMe	4-Cl	4l	82	164–166	–
13	3-OMe	4-Cl	4m	80	159–160	–
14	2-F	4-Cl	4n	88	144–148	–
15	$\text{C}_4\text{H}_3\text{O}$ (furan)	4-Cl	4o	89	144–146	–
16	4-N(Me) ₂	4-Cl	4p	81	139–140	–
17	2-Cl	4-Cl	4q	84	168–170	–

Then in determining the best ammonium source, we found that NH_4OAc produced acetic acid in the reaction conditions that have good effect in progress of the reaction. Therefore, the experimental results convinced us that NH_4OAc is the most effective ammonium source for this transformation. The reaction in the presence of other ammonium sources required longer reaction times, and produced lower yields (Table 3).

The effect of the reaction power was investigated by carrying out model reaction. It was shown that reaction at power of 50 w was found to be optimal (Table 4). The reusability of the catalyst was also investigated. For this purpose, the same model reaction was again studied under optimized conditions. After completion of the reaction, by addition of hot ethanol, insoluble catalyst

was filtered off. Then, catalyst was washed with acetone and dried. It was reused in subsequent reactions without reduction in activity as shown in Table 5. Results showed that nanocrystalline MgAl_2O_4 could be used for five successive runs without significant decrease in its catalytic activity. Finally, to evaluate the generality of this model reaction, we prepared a range of 2,4,6-triarylpyridines under the optimized reaction conditions (Table 6).

Suggested mechanism is shown in Scheme 2. After Aldol condensation of aldehyde and acetophenone, second molecule of acetophenone is condensed by ammonia and forms enamine. The Michael addition of enamine on aldol product and then cyclization produces dihydropyridine. After that, oxidation takes place

Scheme 2. Proposed mechanism of reaction.

simply using the catalyst and affords the final product. Nanocrystalline MgAl_2O_4 facilitates all reaction routes such as Aldol condensation, Michael addition, cyclization and oxidation.

4. Conclusion

In summary, we have reported a one-pot and efficient method for the synthesis of 2,4,6-triarylpyridines using novel and applicable MgAl_2O_4 nanostructures. This protocol provides a very fast, good yield, low pollution, green and low cost procedure for the synthesis of these products. Moreover, the microwave-assisted combustion method is an economical and rapid method for the preparation of triarylpyridines with respect to energy, time and simplicity. We believe that this procedure appears to have an extensive scope with respect to variation in the pyridine 2- or 6- and 4-positions.

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